

REMARKS

Reconsideration and allowance are respectfully requested.

Applicants elected Group III and the species (A) "four plates" and (B) "cysteinyl protease" for examination. Claims 15-20 read on the species elected for examination. Applicants note the Examiner's statement that "cys-protease" is free of prior art and, thus, infer that examination has been expanded to generic limitations (e.g., enzymes, hydrolases, peptidases, proteases, etc.)

Non-elected claims 3-11 and 13-14 were withdrawn from consideration by the Examiner. Applicants have canceled non-elected claims without prejudice to future prosecution of that subject matter.

The amendments are supported by the original disclosure and, thus, no new matter has been added. If the Examiner should disagree, however, she is respectfully requested to point out the challenged limitation with particularity in the next Action so support may be cited in response.

Restriction/Election

This response was initially filed on August 23, 2004. The Examiner mailed an Official Communication on November 16, 2004 and contended that the pending claims are drawn to a non-elected invention and therefore were not responsive. But new claim 15 is readable on the elected invention of Group III because it includes all limitations of the originally elected claim 12. As noted by the Examiner, claim 15 also includes the formula recited in original claim 3 but this is an additional limitation which is directed to the same invention of Group III (i.e., claim 15 is within the scope of elected claim 12). Here, claims 12 and 15 are related as subcombination and combination which should be examined in the same application in accordance with M.P.E.P. § 806.05(c) because there has been no demonstration of two-way distinctness as required by the Manual of Patent Examining Procedure. The Examiner is requested to cite support for her contention that including an additional limitation from a non-elected claim is not authorized.

The inventive concept of original claim 12 now appears in new claim 15 at lines 19 to 25 (albeit with clarification as to the nature of the phrase "variable group" which is

now recited as an amino acid residue A-D in response to the Section 112 rejection to the term "variable"). Similarly, each of the features of original claims 1-2 are incorporated, with minor clarifications, into new claim 15. Accordingly, one would conclude that new claim 15 is within the scope of original claim 12, which is the criterion which ought reasonably to determine whether a new claim is drawn to the elected invention of Group III. In view of the various Section 112 rejections, however, in particular the objection to the phrase "format adapted to allow deduction," it was believed to be useful to comprehensively define the deconvolution strategy in the independent claim, notwithstanding that the deconvolution strategy was regarded as a separate and distinct invention. Here it is being used to better define the invention of original claim 12 instead of as an alternative to the screening method of original claim 2. Similarly, clarity considerations have caused the limitations of original claims 6 and 14 to be incorporated into the new claim 15, while better characterization of the invention against the prior art has motivated bringing a limitation of original claim 3 into new claim 15. But in each case the resultant claim employs the "library variation" concept presented in original claim 12.

Original claim 12 and new claim 15 are both directed to methods of screening for interaction of an enzyme (claim 12 recites "active moiety" and original claim 5 describes "enzyme" as an active moiety) with at least one of a set of peptides (claim 12 recites "compound" and peptides are examples of the compound). Therefore, different types of enzymes are clearly within the scope of the elected invention (either original claim 12 or new claim 15). Cys-protease was elected as the species for examination and, in the absence of prior art teaching the invention with cys-protease, the Examiner should consider the other proteases and the genus "enzyme" in her search.

The pending claims have a narrower scope, in all respects, than the originally elected claim 12 of Group III. Therefore, claims 15-20 should be examined in this application as directed to the invention of Group III.

Specification

An Abstract of the Disclosure is attached hereto. Its entry is requested to comply with the Examiner's requirement. No new matter is added because it is identical to the abstract of parent Int'l Patent Appln. No. PCT/GB97/01158.

This application was filed under 35 U.S.C. 371 with a request to begin national examination and a copy of the International Application. This copy included substitute sheets which appear not to have been reviewed by the Examiner because the copy filed on October 23, 1998 does not refer to Table II (which appears on page 23) and does contain Figure 18 on sheet 17/17 of the drawings. The Examiner is requested to review the file and confirm that the copy of the application being examined is marked "SUBSTITUTE SHEET (RULE 26)" at the bottom of each page of the specification and drawings.

Withdrawal of the objections is requested.

Information Disclosure Statement

An Information Disclosure Statement (IDS) under 37 CFR § 1.97(c), which was comprised of Form PTO-1449, the references submitted for the Examiner's consideration, and the required fee, was submitted on August 23, 2004. Consideration of the IDS and return of an initialed copy of the Form PTO-1449 per M.P.E.P. § 609 are earnestly solicited. A copy of the Form PTO-1449 is enclosed for the Examiner's convenience.

35 U.S.C. 112 – Written Description

The specification must convey with reasonable clarity to persons skilled in the art that applicant was in possession of the claimed invention as of the filing date sought. See *Vas-Cath v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). But the Patent Office has the initial burden of presenting evidence or a reason why persons of ordinary skill in the art would not have recognized such a description of the claimed invention in the original disclosure. See *In re Gosteli*, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989).

Claims 1-2 and 12 were rejected under Section 112, first paragraph, because it was alleged that they contain "subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

inventor(s), at the time the application was filed, had possession of the claimed invention." Applicants traverse.

The claims are directed to linear peptides of natural or non-natural amino acid residues. The peptides are comprised of at least four residues B, C, D and E. All types of variations are not required to practice the claimed invention because there are b variants of amino acid B, c variants of amino acid C, d variants of amino acid D, and e variants of amino acid E. Insoluble peptides are excluded from the claimed invention: variations of the "two amino acid residues" selected from B, C, D or E (or the "other two amino acid residues") which result in a soluble peptide comprise the mixtures making up the set of linear peptides in solution. Similarly, libraries not comprised of a peptide which is an active substrate or inhibitor of the enzyme are excluded from the claimed invention (i.e., there is "at least one" peptide which interacts with the enzyme).

The amino acid sequences of peptides are indexed by their positions (or format) on plates of the L1 and L2 libraries. Certain features of the formatting of libraries which were disclosed in Applicants' specification have now been incorporated into the claimed invention: e.g., indexing of peptides by well position (or formatting) complies with the general deconvolution formulae recited in claim 15. The row and column positions of wells in a plate identify the amino acid sequence of the peptide which interacts with the enzyme. Applicants' experience has been that formatting libraries of linear peptides comprised of at least four amino acid residues in compliance with such formulae avoids the solubility and interaction phenomena cited by the Examiner in reference to Sharma. If this rejection is maintained, the Examiner is requested to provide evidence to support her assertion that libraries formatted in the manner described in claim 15 would suffer from the solubility and interaction phenomena discussed in the Office Action.

Withdrawal of the written description rejection made under Section 112, first paragraph, is requested because the specification conveys to a person skilled in the art that Applicants were in possession of the claimed invention as of the filing date.

35 U.S.C. 112 – Definiteness

Claims 1-2 and 12 were rejected under Section 112, second paragraph, as being allegedly "indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Applicants traverse.

The terms "adapted" and "active" are not recited in the claims. The term "unique" as used in the claims is clear in its context. The autodeconvolution strategy disclosed in Applicants' specification requires "placing the mixtures of peptides separately each into individual wells positioned on plates" of the L1 and L2 libraries. Peptides in an individual well have amino acid sequences with common residues at two positions (i.e., "all variations") and non-common residues at the other two positions (i.e., "a unique pair"). So uniqueness is characterized by the degree of variation at those positions.

Method steps are recited in claim 15. The Examiner is thanked for her suggesting the alternative term "at least one" which is now recited.

Limitation of the peptides to those comprised of at least four amino acid residues of the formula —Bb—Cc—Dd—n(Ee)— and incorporating their definitions into claim 15 clarifies the combinatorial libraries being screened.

Applicants request withdrawal of the Section 112, second paragraph, rejection because the pending claims are clear and definite.

35 U.S.C. 102 – Novelty

A claim is anticipated only if each and every limitation as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of Calif.*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The identical invention must be shown in as complete detail as is claimed. See *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Claims 1-2 and 12 were rejected under Section 102(b) as allegedly anticipated by Deprez et al. (J. Am. Chem. Soc. 117:5405-5406, 1995). Applicants traverse. As an initial matter, the Examiner refers to "the alternative rejection" on page 8 of the Action but it is not clear what is meant because there only one prior art rejection was made.

Deprez et al. disclose combinatorial libraries of trimer peptides whereas the claimed invention requires at least 4-7 mers, which immediately increases the degree of complexity of constructing combinatorial libraries. Note also that Deprez et al. do no describe placing mixtures of peptides in wells of plates and identifying peptides which interact with enzyme by the well positions of those peptides.

The claimed invention requires indexing peptides of the combinatorial library in, for example, conventional formats of plates (e.g., 96-wells, 384-wells) in such a way that the library can be readily deconvoluted with only two sets of plates (i.e., from L1 and L2 libraries). In contrast, Deprez et al. disclosed using large numbers of trimers per mixture (125 trimers) which would rapidly become unfeasible in the small volumes of wells in plates. Accordingly, Deprez et al. do not suggest the solution discovered by Applicants to the problem of deconvoluting complex libraries.

Withdrawal of the Section 102 rejection is requested because all limitations of the claimed invention are not disclosed by the cited reference.

Conclusion

Having fully responded to all of the pending objections and rejections contained in this Office Action, Applicants submit that the claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if any further information is required.

Respectfully submitted,

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